

WHAT IS CLAIMED IS:

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1. A method of cloning a porcine fetus or live offspring, comprising:
 - (i) inserting a desired differentiated pig cell or cell nucleus into an optionally enucleated pig oocyte or blastomere, under conditions suitable for the formation of a nuclear transfer (NT) unit;
 - (ii) removing the endogenous nucleus from said oocyte or blastomere if not previously removed;
 - (iii) activating the resultant nuclear transfer unit;
 - (iv) optionally culturing said NT unit; and
 - (v) transferring said optionally cultured NT unit to a host mammal such that the NT unit develops into a porcine fetus or animal.
2. The method according to Claim 1, which results in a live offspring.
3. The method according to Claim 1, wherein a desired DNA is inserted, removed or modified in said differentiated pig cell or cell nucleus, thereby resulting in the production of a genetically altered NT unit.
4. The method according to Claim 3, which further comprises developing the fetus to an offspring.

5. The method according to Claim 1, which comprises culturing said activated nuclear transfer unit until greater than the 2-cell developmental stage.

6. The method of Claim 1, wherein the transferred NT unit is one cell.

7. The method of Claim 6, wherein transfer is effected on the same day as activation.

8. The method of Claim 1, wherein the oocyte is enucleated after introduction of said differentiated cell or nucleus.

9. The method of Claim 1, wherein the differentiated cell or nucleus is that of a proliferating (non-quiescent) cell.

10. The method of Claim 9, wherein said differentiated cell is in G₁, G₂ or M.

11. The method of Claim 1, wherein the pig oocyte is matured *in vitro*.

12. The method of Claim 1, wherein the pig oocyte is matured *in vivo*.

13. The method of Claim 1, wherein said differentiated pig cell or nucleus is obtained from a somatic cell.

14. The method of Claim 1, wherein said differentiated pig cell or nucleus is obtained from a germ cell.

15. The method of Claim 1, wherein the host animal comprises one or more helper embryos.

16. The method of Claim 1, wherein the differentiated cell comprises one or more genetic modifications that inhibit rejection upon implantation of cells, tissues, or organs of said cloned fetus or animal in a human.

17. The method according to Claim 1, wherein the differentiated pig cell or cell nucleus is derived from mesoderm.

18. The method according to Claim 1, wherein the differentiated pig cell or cell nucleus is derived from ectoderm.

19. The method according to Claim 1, wherein the differentiated pig cell or cell nucleus is derived from endoderm.

20. The method according to Claim 1, wherein the differentiated pig cell or cell nucleus is a fibroblast cell or cell nucleus.

21. The method according to Claim 1, wherein the differentiated pig cell or cell nucleus is an adult differentiated cell or nucleus derived therefrom.

22. The method according to Claim 1, wherein the differentiated pig cell or cell nucleus is an embryonic or fetal cell or cell nucleus.

23. The method according to Claim 1, wherein the differentiated pig cell or nucleus is a proliferating cell obtained directly from a pig.

24. The method of Claim 1, wherein said differentiated cell or nucleus is obtained from a proliferating cell that has been expanded in tissue culture.

25. The method of Claim 1, wherein said differentiated cell or nucleus is proliferated *in vivo*, prior to nuclear transfer.

26. The method of Claim 25, wherein said proliferating pig cell is obtained from a SCID mouse which has been injected with porcine cells.

27. The method of Claim 25, wherein said proliferating cell has been genetically modified.

28. The method of Claim 27, wherein said genetic modification is effected by use of a recombinant virus, viral vector, naked DNA, or plasmid vector.

29. The method according to Claim 1, wherein the enucleated oocyte is matured prior to enucleation.

546a3 30. The method according to Claim 1, wherein the fused nuclear transfer unit is activated by exposure to a single or multiple electrical pulses.

31. The method according to Claim 1, wherein the fused nuclear transfer unit is activated by exposure to ionomycin and DMAP.

32. The method according to Claim 1, wherein the fused nuclear transfer unit is activated by exposure to at least one activating factor derived from sperm cells.

33. The method according to Claim 3, wherein microinjection is used to insert said heterologous DNA.

34. The method according to Claim 3, wherein electroporation is used to insert a heterologous DNA.

35. A cloned, optionally transgenic porcine fetus or animal obtained according to the method of Claim 1, wherein said fetus or animal has the same genotype as a previously existing non-embryonic differentiated porcine cell which is optionally genetically modified.

sub 24 → 36. The method according to Claim 1, which further comprises combining the cloned NT unit with a fertilized embryo to produce a chimeric embryo.

37. The method according to Claim 36, which includes developing the chimeric embryo to an offspring.

38. A chimeric fetus obtained according to the method of Claim 36.

39. A chimeric offspring obtained according to the method of Claim 37.

40. Progeny of the chimeric offspring according to Claim 39.

sub 25 → 41. A method of producing a porcine CICM (pluripotent) cell line, comprising:

- (i) inserting a desired differentiated pig cell or cell nucleus into an optionally enucleated pig oocyte, under conditions suitable for the formation of a nuclear transfer (NT) unit;
- (ii) removing the endogenous oocyte nucleus if not already effected;
- (iii) activating the resultant nuclear transfer unit; and
- (iv) culturing cells obtained from said cultured NT unit to obtain a pig CICM cell line, which is pluripotent and may be maintained indefinitely in tissue culture.

42. The method of Claim 41, which comprises culturing said activated nuclear transfer unit until a discernible trophectoderm and inner cell mass is obtained.

43. A CICM cell line obtained according to the method of Claim 41, wherein said cell line is pluripotent and comprises the same genotype as a previously existing, non-embryonic differentiated cell.

44. The method according to Claim 41, wherein a desired DNA is inserted, removed or modified in said differentiated pig cell or cell nucleus, thereby resulting in the production of a genetically altered NT unit.

45. A transgenic CICM cell line obtained according to Claim 44, wherein said cell line has the identical genotype as a previously existing porcine differentiated cell that has been genetically modified.

46. The method of Claim 41, wherein the resultant CICM cell line is induced to differentiate.

47. The method of Claim 44, wherein the CICM cell is allowed to differentiate.

~~48. Differentiated cells obtained by the method of Claim 46.~~

49. A method for cloning a porcine fetus or live offspring comprising the following steps:

- (i) activating a porcine oocyte that optionally is enucleated;
- (ii) transferring a desired differentiated pig cell or nucleus into said porcine oocyte after or proximately simultaneous to said activating step (i) to produce a NT unit;
- (iii) removing the endogenous oocyte nucleus if oocyte not previously enucleated; and
- (iv) transferring said NT unit, optionally after a culturing step, into a female porcine to produce a porcine fetus or animal.